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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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OBLON, SPIVAK, MCCLELLAND, MAIER & NEUSTADT, P.C.
1940 DUKE STREET
ALEXANDRIA, VA 22314

EXAMINER	
FRONDA, CHRISTIAN L	
ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 05/19/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/919,891	BATHE ET AL.	
	Examiner	Art Unit	
	Christian L Fronda	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 March 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-34* is/are pending in the application.

4a) Of the above claim(s) *7 and 10-34* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,5,8 and 9* is/are rejected.

7)☒ Claim(s) *4 and 6* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *02 August 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *11/01; 2/02; 6/03*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restriction

1. Applicants' election with traverse of Group I, claims 1-6, 8, and 9 in the **RESPONSE TO RESTRICTION REQUIREMENT** dated March 01, 2004 is acknowledged.

The traversal is on the grounds that insufficient reasons have been stated to sustain the Restriction Requirement. This is not found persuasive because as stated in the previous Office Action each of the products of Groups I, II, and V are independent chemical entities and require different literature searches and each of the processes of Groups III, IV, and VI are distinct both physically and functionally and require different process steps, reagents, and parameters. The product of Groups II can be used in a process that is materially different from the process of Groups III and IV such as using coryneform bacteria in a recombinant process for the production of the enhanced metH protein. The product of Groups I can be used in a process that is materially different from the process of Group VI such as using the polynucleotide in a recombinant process for the production of homocysteine methyltransferase II.

The requirement is still deemed proper and is therefore made FINAL.

2. Claims 1-6, 8, and 9 are under consideration in this Office Action.

Claim Rejections - 35 U.S.C. § 112, 1st Paragraph

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 1-3, 5, and 8 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claimed invention encompass any polynucleotide that is at least 70% identical to a polynucleotide encoding a polypeptide that comprises the amino acid sequence of SEQ ID NO: 2, a polynucleotide that encodes a polypeptide that is at least 70% identical to the amino acid

sequence of SEQ ID NO: 2, and a polynucleotide containing at least 15 successive nucleotides thereof. The specification, however, only provides the following representative species encompassed by the invention: an isolated polynucleotide consisting of SEQ ID NO: 1. There is no disclosure of any particular structure to function/activity relationship in the single disclosed species. The specification also fails to describe additional representative species of these polynucleotides by any identifying structural characteristics or properties for which no predictability of structure is apparent. Given this lack of additional representative species as encompassed by the claims, Applicants have failed to sufficiently describe the claimed invention, in such full, clear, concise, and exact terms that a skilled artisan would recognize Applicants were in possession of the claimed invention. Claims 2, 3, 5, and 8 which depend from claim 1 are also rejected because they do not correct the defect of claim 1.

5. Claims 1-3, 5, and 8 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated polynucleotide encoding a polypeptide comprising the amino acid sequence of SEQ ID NO:2 or an isolated polynucleotide comprising SEQ ID NO: 1; does not reasonably provide enablement for any other embodiment.

Factors to be considered in determining whether undue experimentation is required, are summarized In re Wands [858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)]. The Wands factors are: (a) the quantity of experimentation necessary, (b) the amount of direction or guidance presented, (c) the presence or absence of working example, (d) the nature of the invention, (e) the state of the prior art, (f) the relative skill of those in the art, (g) the predictability or unpredictability of the art, and (h) the breadth of the claim.

The nature and breadth of the claims encompass any polynucleotide that is at least 70% identical to a polynucleotide encoding a polypeptide that contains the amino acid sequence of SEQ ID NO: 2 , a polynucleotide that encodes a polypeptide that is at least 70% identical to the amino acid sequence of SEQ ID NO: 2, and a polynucleotide containing at least 15 successive nucleotides thereof

The specification provides guidance and examples for making an isolated polynucleotide encoding a polypeptide comprising the amino acid sequence of SEQ ID NO:2 or an isolated polynucleotide comprising SEQ ID NO: 1. However, the specification does not teach the specific structural/catalytic amino acids and the structural motifs essential for protein activity/function which cannot be altered. The state of the art as exemplified by Attwood et al. (Comput. Chem. 2001, Vol. 25(4), pp. 329-39) is such that "...we do not fully understand the rules of protein folding, so we cannot predict protein structure; and we cannot invariably diagnose protein function, given knowledge only of its sequence or structure in isolation" (see Abstract and entire publication). Furthermore, Ponting (Brief. Bioinform. March 2001, Vol. 2(1), pp. 19-29) states that "...predicting function by homology is a qualitative, rather than quantitative, process and requires particular care to be taken...due attention should be paid to all

available clues to function, including orthologue identification, conservation of particular residue types, and the co-occurrence of domains in proteins" (See Abstract and entire publication).

The standard for meeting the enablement requirement is whether one of skill in the art can make the invention without undue experimentation. The amount of experimentation to make the claimed polynucleotide is enormous and entails selecting specific nucleotides to change (deletion, insertion, substitution, or combinations thereof) in a polynucleotide to make a polynucleotide that encodes a polypeptide that contains an amino acid sequence that is at least 70% identical to SEQ ID NO: 2 and determining by assays whether the polypeptide has activity. The specification does not provide guidance with respect to the specific structural/catalytic amino acids and the structural motifs essential for enzyme structure and activity/function which must be preserved. Thus, searching for the specific nucleotides to change (deletion, insertion, substitution, or combinations thereof) in a polynucleotide to make a polynucleotide that encodes a polypeptide that contains an amino acid sequence that is at least 70% identical to SEQ ID NO: 2 is well outside the realm of routine experimentation and predictability in the art of success in determining whether the resulting polypeptide has activity is extremely low since no information is provided by the specification regarding the specific catalytic amino acids and the structural motifs essential for enzyme structure and activity/function which must be preserved.

The Examiner finds that one skilled in the art would require additional guidance, such as information regarding the specific catalytic amino acids and the structural motifs essential for activity/function which must be preserved. Without such a guidance, the experimentation left to those skilled in the art is undue. Claims 2, 3, 5, and 8 which depend from claim 1 are also rejected because they do not correct the defect of claim 1.

6. Claim 9 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

It is apparent that the *E.coli* DSM14354 is required to practice the claimed invention. As such the *E.coli* DSM14354 must be readily available or obtainable by a repeatable method set forth in the specification, or otherwise readily available to the public. If it is not so obtainable or available, the requirements of 35 USC § 112, first paragraph, may be satisfied by a deposit of the *E.coli* DSM14354.

The process disclosed in the specification to make the *E.coli* DSM14354 does not appear to be repeatable. The specification discloses a gene and plasmid vectors used to construct the *E.coli* DSM14354. However, the nucleotide sequences of the plasmid vectors are not fully disclosed, nor have all the nucleotide sequences required for their construction been shown to be biblically known and freely available. The specification does not disclose a repeatable process to obtain the plasmid vectors and it is not apparent if the nucleotide sequences of the gene and novel vectors are readily available to the public. It is not apparent if the *E.coli* DSM14354 or

source material to make the *E.coli* DSM14354 are both known and readily available to the public.

Applicants' referral to deposit of *E.coli* DSM14354 on page 19, lines 8-12, in the specification is noted but is considered insufficient assurance that all of the conditions of 37 CFR 1.801-1.809 have been met. While Applicants have deposited the *E.coli* DSM14354, there is no indication in the specification as to public availability.

If the deposit is made under the terms of the Budapest Treaty, then an affidavit or declaration by the applicant, or a statement by an attorney of record over his/her signature and registration number, stating that the specific microorganism has been deposited under the Budapest Treaty and that the strain will be irrevocably and without restriction or condition released to the public upon the issuance of the patent, would satisfy the deposit requirement made herein.

If the deposit has not been made under the Budapest Treaty, then in order to certify that the deposit meets the criteria set forth in 37 C.F.R. 1.801-1.809 and MPEP 2402-2411.05, the applicant may provide assurance or compliance by an affidavit or declaration, or by a statement by an attorney of record over his/her signature and registration number, showing that:

(1) during the pendency of this application, access to the invention will be afforded to the Commissioner upon request;

(2) all restriction upon availability to the public will be irrevocably removed upon granting of the patent;

(3) the deposit will be maintained in a public repository for a period of 30 years or 5 years after the last request or for the effective life of the patent, whichever is longer; and

(4) the deposit will be replaced if it should ever become inviable.

Claim Rejections - 35 U.S.C. § 112, 2nd Paragraph

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 1-3, 5, and 8 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is vague and indefinite because the specific nucleotide sequence to which the claimed polynucleotide has 70% identity to is not known and not defined in the specification. Claims 2, 3, 5, and 8 which depend from claim 1 is also rejected because they do not correct the

defect of claim 1.

In claim 5 ii), the phrase "within the range of the degeneration of the genetic code" renders the claim vague and indefinite because the meaning of the phrase is not known and not defined in the specification. In part (iii), the hybridization conditions are not recited and not known and thus render the claim vague and indefinite. In part (iv) the phrase " sense mutations of neutral function" is vague and indefinite because the meaning of the phrase is not known and not defined in the specification.

Claim Rejections - 35 U.S.C. § 102

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

10. Claims 1 and 2 are rejected under 35 U.S.C. 102(b) as being anticipated by Eiglmeier et al. (GenBank Accession AL023591).

Eiglmeier et al. (GenBank Accession AL035310) teach a polynucleotide that contains at least 15 successive nucleotides encoding SEQ ID NO: 2 (see attached alignment). Thus, the reference teachings anticipate the of claimed invention.

11. Claim 5 is rejected under 35 U.S.C. 102(b) as being anticipated by Strausberg (Accession AW576625).

Strausberg (Accession AW576625) teach a polynucleotide that is expected to hybridize to SEQ ID NO: 1 since no stringent hybridization conditions have been recited (see attached alignment). Thus, the reference teachings anticipate the of claimed invention.

Conclusion

12. No claim is allowed.

13. Claims 4 and 6 are objected to as being dependent upon a rejected base claim, but would

be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christian L Fronda whose telephone number is (571)272-0929. The examiner can normally be reached Monday-Friday between 9:00AM - 5:00PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura N Achutamurthy can be reached on (571)272-0928. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

CLF

PONNATHAPURA ACHUTAMURTHY
SUPERVISORY PATENT EXAMINER